



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/767,538	01/23/2001	Yingjian Wang	17281/00002	2993

Yingyi Wang  
Hypromatrix , Inc.  
100 Barber Avenue  
Worcester, MA 01606

7590

07/20/2010

EXAMINER
----------

LUNDGREN, JEFFREY S

ART UNIT	PAPER NUMBER
----------	--------------

1639

MAIL DATE	DELIVERY MODE
-----------	---------------

07/20/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.



UNITED STATES PATENT AND TRADEMARK OFFICE

---

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Application Number: 09/767,538  
Filing Date: January 23, 2001  
Appellantss: WANG ET AL.

---

Mr. Yingyi Wang  
For Appellants

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed May 26, 2010, appealing from the Office action mailed May 24, 2006.

Art Unit: 1639

**(1) Real Party of Interest**

The real party of interest is identified in the Appeal Brief.

**(2) Related Appeals and Interferences**

The Examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The following is a list of claims that are rejected and pending in the application:

Claims 1-46 and 49-53 are pending in the instant application.

Claims 1-36, 40-42 and 50-52 are withdrawn from consideration.

Claims 37-39, 43-46, 49 and 53 stand rejected.

**(4) Status of Amendments After Final**

The Examiner has no comment on the Appellantss' statement of the status of amendments after final rejection contained in the Brief.

**(5) Summary of Claimed Subject Matter**

The Examiner has no comment on the summary of claimed subject matter contained in the Brief.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The Examiner has no comment on the Appellantss' statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office Action from which the Appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

Art Unit: 1639

### (7) Claims Appendix

The Examiner has no comment on the copy of the appealed claims contained in the Appendix to the Appellant's brief.

### (8) Evidence Relied Upon

U.S. Patent No. 6,365,349, issued April 2, 2002, to Moyhihan *et al.*;

U.S. Patent No. 6,083,763, issued July 4, 2000, to Balch;

U.S. Patent No. 5,700,906, issued on December 23, 1997, to Arnot *et al.*; and  
Reek *et al.*, *BioTechniques* 19:282, (1995).

### (9) Grounds of Rejection

The following grounds of rejection are applicable to the appealed claims:

#### 9.1 Claims 37-39, 43-46 and 53 are anticipated by Moynihan:

Claims 37-39, 43-46 and 53 are rejected under 35 U.S.C. § 102(e) as being anticipated by Moynihan *et al.*, U.S. Patent No. 6,365,349 B1, issued on April 2, 2002, having priority to July 22, 1997.

Claim 37 is directed to a method of bringing two or more reagents into contact with one or more biological targets, comprising an array of reagents contacting a group of biological targets on cell growth support, wherein the reagents locations are addressed.

Moynihan teaches an improved pipette dispenser for use in biological assays in array format. Moynihan teaches that her invention is relevant to the combinatorial arts for the testing of many samples (*i.e.*, two or more reagents):

***“In the fields of molecular biology and microbiology it has long been common in the art to make replicate arrays of biological agents to facilitate parallel testing of many samples. For example, the use of sterile velvet cloths and a piston-ring apparatus has long been used to make replicate agar plates of bacterial and yeast colonies on many plates, each containing a *different growth medium*, as a way of rapidly screening a large number of independent colonies *for different growth phenotypes* (Lederberg and Lederberg, J. Bacteriol. 63:399, 1952). Likewise, 96-well microtiter plates have long been used to store, in an organized and easily accessed fashion, large numbers of cell lines and virus isolates***

Art Unit: 1639

***representing recombinant DNA libraries or monoclonal antibody cell lines.”***

Moynihan, col. 1, lines 20-34 (emphasis added).

Moynihan discloses a well-known apparatus in the art for dispensing the reagents to the array for delivery the two or more reagents:

***“As noted above, transfer devices have been in use for some time in the fields of microbiology and molecular biology. The types of devices which have been used can be roughly divided into two categories. Pressure devices (e.g., pumps and automatic pipettes), driven by positive and/or negative pressure, which deliver fixed aliquots of liquids sample via a pipette tip to a solid surface or into a microtiter well. Pipette arrays have been constructed that correspond to the standard 96-well microtiter dish format (Reek *et al.*, BioTechniques 19:282, 1995). These devices are most accurate in the 5 µl and above volume range, but are generally ill-suited to smaller volume tasks.”***

Moynihan, col. 3, lines 1-13 (emphasis added). The pipettes comprise “barriers” as claimed by Applicants, as Applicants’ claims are open to the physical geometries of the barriers.

Claim 38 is directed to an array that comprises two or more reagents, wherein at least one reagent portion comprises two or more reagents, and claim 39 is directed to a reagent of DNA; Moynihan teaches these limitations in that the two or more reagents in one of the reagent portions (see section titled *Biomolecule Solutions*; col. 7, line 25-58; *i.e.*, water, an oligonucleotide, and a thickening agents – three reagents in one pipette). Claim 43 is directed to a substantially level surface so that the reagent portions do not commingle; see the pipette arrays as disclosed by Moynihan above, wherein each pipette prevents commingling. Claim 44 is directed to supports comprising solid supports of rigid plastic plates, and claim 45 is directed to a support that comprises a layer of one or more polymers adapted to immobilize one or more reagents; Moynihan teaches pipette arrays (*i.e.*, plastic or glass, wherein the plastic pipettes comprise at least one layer of a polymer)<sup>1</sup>. Claim 46 is directed to seeding two or more cells;

---

<sup>1</sup> One of ordinary skill in the would at once envisage this limitation because plastic pipette tips are well-known and routine in the art of laboratory preparations. See *In re Graves*, 69 F.3d 1147, 36 USPQ2d 1697 (Fed. Cir. 1995), where prior art reference disclosing a system for testing the integrity of electrical interconnections that did not specifically disclose simultaneous monitoring of output points still anticipated claimed invention because simultaneous monitoring was within the knowledge of a skilled artisan; see also *In re Donohue*, 766 F.2d 531, 533 (Fed. Cir. 1985), where prior art anticipates a claim if it discloses the claimed invention such that a skilled artisan

Art Unit: 1639

Moynihan teaches cells in growth medium in a 96-well microtiter plate (col. 3, lines 23-47). Claim 53 is directed to separating the array from the cell growth medium; in Moynihan's pipette array (with reference to Reek *et al.*)<sup>2</sup>, after the automated pipette array moves close to the cell growth medium and deposits the solution near the cell growth medium, it is then separated from the cell growth support.

9.2 Claims 37-39, 43-46, 49 and 53 are obvious over Balch and Moynihan:

Claims 37-39, 43-46, 49 and 53, are rejected under 35 U.S.C. 103(a)<sup>3</sup> as being unpatentable over Balch, U.S. Patent No. 6,083,763, issued on July 4, 2000, in view of Moynihan *et al.*, U.S. Patent No. 6,365,349 B1, issued on April 2, 2002.

The limitations of claims 37-39, 43-46 and 53 have been detailed above, and are herein incorporated by reference to the instant rejection.

Claim 49 is directed to a step of applying electric pulses to apply one or more reagents.

Balch teaches a method and apparatus for analyzing molecular structures within a sample substance using an array having a plurality of test sites upon which the sample substance is applied. The invention is also directed to a method and apparatus for constructing molecular arrays having a plurality of test sites. The invention allows for definitive high throughput analysis of multiple analytes in complex mixtures of sample substances. A combinatorial analysis process is described that results in the creation of an array of integrated chemical

---

could take the teaching and his own knowledge to possess the claimed invention; see also *In re Best* 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Evidence that plastic pipettes are well-known and routine in the art of laboratory preparations is common knowledge to those of ordinary skill can be illustrated by numerous teachings, for example, the Arnot reference (see Example 7; Arnot *et al.*, U.S. Patent No. 5,700,906, issued on December 23, 1997).

<sup>2</sup> One of ordinary skill in the art would incorporate the teachings of Reek into Moynihan, in particular the teachings as it pertains to automated pipette array, and therefore is treated as teaching these limitations. See, *Advanced Display Systems Inc. v. Kent State University*, 54 USPQ2d 1673 at 1679 (Fed. Cir. 2000) – "Incorporation by reference provides a method for integrating material from various documents into a host document --a patent or printed publication in an anticipation determination by citing such material in a manner that makes clear that the material is effectively part of the host document as if it were explicitly contained therein. See *General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USPQ 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967).

Art Unit: 1639

devices. These devices operate in parallel, each unit providing specific sets of data that, when taken as a whole, give a complete answer for a defined experiment. This approach is uniquely capable of rapidly providing a high density of information from limited amounts of sample in a cost-effective manner. One of the embodiments of the method/apparatus, relates to an array of dispensing units, wherein electric pulses are used to dispense reagents from array to the substrate (col. 11, lines 33-54); as in claim 49. The limitations of claims 44-46 are also met by the teachings of Balch (col. 12, lines 42-67).

Although Balch teaches the fabrication of arrays of biological materials and assays using an automated array dispensing device, Balch does not explicitly teach the application of assays with his array to substrates have cell growth medium as in claim 37.

Moynihan teaches an improved pipette dispenser for use in biological assays in array format. Moynihan teaches that her invention is relevant to the combinatorial arts for the testing of many samples (*i.e.*, two or more reagents):

***“In the fields of molecular biology and microbiology it has long been common in the art to make replicate arrays of biological agents to facilitate parallel testing of many samples.*** For example, the use of sterile velvet cloths and a piston-ring apparatus has long been used to make replicate agar plates of bacterial and yeast colonies on many plates, each containing a ***different growth medium***, as a way of rapidly screening a large number of independent colonies for different growth phenotypes (Lederberg and Lederberg, J. Bacteriol. 63:399, 1952). ***Likewise, 96-well microtiter plates have long been used to store, in an organized and easily accessed fashion, large numbers of cell lines and virus isolates representing recombinant DNA libraries or monoclonal antibody cell lines.***”

Moynihan, col. 1, lines 20-34 (emphasis added).

Moynihan discloses a well-known apparatus in the art for dispensing the reagents to the array for delivery the two or more reagents:

***“As noted above, transfer devices have been in use for some time in the fields of microbiology and molecular biology.*** The types of devices which have been used can be roughly divided into two categories. Pressure devices (e.g., pumps and automatic pipettes), driven by positive and/or negative pressure, which deliver fixed aliquots of liquids sample

---

Art Unit: 1639

via a pipette tip to a solid surface or *into a microtiter well*. *Pipette arrays* have been constructed *that correspond to the standard 96-well microtiter* dish format (Reek *et al.*, BioTechniques 19:282, 1995). These devices are most accurate in the 5  $\mu$ l and above volume range, but are generally ill-suited to smaller volume tasks.”

Moynihan, col. 3, lines 1-13 (emphasis added). The pipettes comprise “barriers” as claimed by Applicants, as Applicants’ claims are open to the physical geometries of the barriers.

Claim 38 is directed to an array that comprises two or more reagents, wherein at least one reagent portion comprises two or more reagents, and claim 39 is directed to a reagent of DNA; Moynihan teaches these limitations in that the two or more reagents in one of the reagent portions (see section titled *Biomolecule Solutions*; col. 7, line 25-58; *i.e.*, water, an oligonucleotide, and a thickening agents – three reagents in one pipette). Claim 43 is directed to a substantially level surface so that the reagent portions do not commingle; see the pipette arrays as disclosed by Moynihan above. Claim 44 is directed to supports comprising solid supports of rigid plastic plates, and claim 45 is directed to a support that comprises a layer of one or more polymers adapted to immobilize one or more reagents; Moynihan teaches pipette arrays (*i.e.*, plastic plates or glass plates, wherein the plastic pipettes comprise at least one layer of a polymer). Claim 46 is directed to seeding two or more cells; Moynihan teaches cells in growth medium in a 96-well microtiter plate (col. 3, lines 23-47). Claim 53 is directed to separating the array from the cell growth medium; in Moynihan’s pipette array (with reference to Reek *et al.*), after the automated pipette array moves close to the cell growth medium and deposits the solution near the cell growth medium, it is then separated from the cell growth support.

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Balch and Moynihan teach laboratory based assays *via* the use of automated, array-based fluid deposition apparatus. One of ordinary skill in the art would have been motivated to extend the application of Balch’s apparatus to cell-based assays because of their importance in the art, such as drug discovery as taught by Moynihan. Accordingly, the invention as a whole was *prima facie* obvious at the time it was invented.

## **(10) Response to Argument**

### *10.1 Response to Appellantss' arguments regarding the rejection over Moynihan:*

Appellants argues that the rejection of the claims as being anticipated by Moynihan is improper, and states that claim 37 is not fully taught. Appellants acknowledges that Moynihan is directed to a pipette dispenser, but mistakenly asserts that the claim does not read on Moynihan because the Moynihan arrays and uses are "very different from the arrays of Claim 37" (Brief, page 18, second paragraph).

The Examiner disagrees. The instantly claimed invention is broad and does read on Moynihan. Appellants does not adequately differentiate the claimed invention from the teachings in Moynihan.

The "different growth medium" of Moynihan meets the limitations of the reagent dissociating from the reagent portions and transferring to the corresponding biological target of the claim (*i.e.*, growth medium feeds the cells). This section of Moynihan is referring to an array of cells that are spatially separated on an array of different growth media, and the cells are screened to determine the properties of the different growth media by the response of the cells.

Appellants also asserts that the method and device of Moynihan can not be used with the method of claim 37, and states:

"The method of cell culture as taught by Moynihan can not be used in the method of Claim 37. In the method of Moynihan cells are seeded on solid support (e.g. 96-well microtiter plates) and generally they can not be used in the method of Claim 37. Only cells seeded on a cell support in specific ways can be used in the method of Claim 37 (see the instant Application, page 26 line 3 to page 28 line 16)."

Brief, page 13, second paragraph.

The Examiner disagrees for the reasons set forth in the rejection above, and is unconvinced by Appellantss' unsupported statement that only cells that are seeded on a cell support in "specific ways" can be used with the method of claim 37. Regarding claim 53, this limitation is addressed in the rejection above. Further evidence of its teaching is found in Reek, which has been incorporated by reference. Reek shows the removal of the growth medium from the array for the screening assay (see Figure 1 on page 284).

Accordingly, the rejection is maintained.

*10.2 Response to Appellantss' arguments regarding the rejection over Balch and Moynihan:*

Although the rejection of the claimed invention is based on the combination of Balch in view of Moynihan, Appellants alleges that the reference of Balch does not teach each and every limitation of claim 37 (Brief, page 15, last paragraph).

The Examiner disagrees, as the instant rejection is based on a combination of the teachings of Balch and Moynihan. The deficiencies of Balch are met by Moynihan for the reasons detailed in the rejection above.

Appellants also alleges that the electric pulses of Balch are not the same electric pulses of claim 37, as the electric pulses of claim 37 are used for transfecting the cells, and not dispensing reagent (Brief, page 16, under item 2). Appellants further suggests that the combination of reference is generally improper because claim 37 is directed towards transfecting cells (Brief, beginning on page 16, under item 3).

The Examiner disagrees. First, claim 37 does not require an electric pulse limitation. Second, the electric pulse limitation of claim 49 is not limited to transfecting cells, but to dispensing reagents, as done in Balch. Additionally, claim 37 is not limited to transfection cells, but instead reads much more broadly, and encompasses the introduction of growth medium nutrients to cells that are plated on thereon.

Appellants alleges that there is no reason to combine the references because neither teaches cells on arrays, and alleges that neither is directed to transfection.

The Examiner disagrees. Moynihan clearly recognizes early uses of arrays of cell plated on media for growing and screening various growth media, and recognizes the use of improved robotics for numerous array-based assays.

Accordingly, the rejection is proper and is therefore maintained.

Art Unit: 1639

**(11) Related Proceeding(s) Appendix**

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this Examiner's Answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Jeffrey S. Lundgren/

Primary Examiner, Art Unit 1639

Conferees:

/ Christopher S. F. Low /

Supervisory Patent Examiner, Art Unit 1639

/GARY BENZION/

Supervisory Patent Examiner, Art Unit 1637